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VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/380,760	11/29/99	BROWN S	620-77

HM12/0310

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EXAMINER	
ZEMAN, R	
ART UNIT	**PAPER NUMBER**
1645	6

DATE MAILED: 03/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/380,760	Brown et al.
Examiner	**Group Art Unit**
Robert A. Zeman	1645

☒ Responsive to communication(s) filed on *Nov 29, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *1.5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Notice to Comply... SEQ

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-20 are pending and under examination.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1645.

This application contains sequence disclosures (see pages 20 and 21) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply. Applicant is requested to return a copy of the attached Notice to Comply with the response. Applicant is given the same period in which to comply with the sequence rules as is available to reply to this action.

Specification

The specification is objected to for the following reason(s):

The brief description of Drawings should be labeled as such. Appropriate correction is required.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

Claims 8-11 and 13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 8-11 and 13 are drawn to a substance with various intended uses. Since intended use carries no patentable weight, said claims do not further limit the scope of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is "undue", not "experimentation" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The aforementioned claims all require a "substance". As written, this term encompasses all types of materials including chemicals and other nonbiologicals and consequently the claims are excessively broad. The specification describes the utilization of proteins in the claimed invention and the provided example is drawn to the use of a small family of proteins (see page 34 lines 3-13 , lines 25-28 and page 35, lines 18-23). However, the specification fails to address the

utilization of other "substances" such as DNA, RNA, organic solvents etc. As such the quantity of experimentation necessary would be extreme due to the lack of guidance provided by Applicant. Additionally, due to the wide variation in the chemical and physical properties of the various materials that are encompassed under the term "substance", it would be impossible for one of skill in the art to predict which "substances" could be used in the claimed invention.

Claims 1, 2, 7, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The aforementioned claims all recite the terms "homologue there of" or "derivative thereof" regarding ICP34.5, PCNA, and GADD34. As written, these terms are excessively broad since Applicant fails to adequately define either term in the specification. As such the quantity of experimentation necessary would be extreme due to the lack of guidance provided by Applicant. Additionally, due to said lack of guidance in describing what constitutes a "derivative" or "homologue", it would be impossible for one of skill in the art to predict what would fall under the category of "derivatives" or "homologues".

Claims 19 and 20 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification at pages 4-5 discloses that a human

GADD34 homologue having one or more of a list of features is to be identified. Claims 19 and 20 are drawn to a human GADD34 homologue which has the entire list of features. The specification does not reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Use of the term "capable of " renders claims 1, 7 and 14 vague and indefinite. Having the "capability" to do something does not mean that it is actually done. Consequently it is impossible to determine the metes and bounds of the claimed invention.

Claims 1, 3, 6, and 14 are rendered vague and indefinite by the use of the term "disrupt(ing)". It is unclear what Applicant is claiming. What constitutes disruption? Total prevention of binding? Partial prevention? Is there a baseline level? Additionally, Applicant recites the simultaneous addition of the first component, second component, and the "substance" being evaluated. The ability of said substance to "disrupt" the interaction between the first and second components is subsequently measured. If all components are mixed simultaneously the

"substance" cannot disrupt the interaction between the first and second components, it can merely prevent said interaction. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Claims 1, 2, 6, 7, 12 and 14 are rendered vague and indefinite through the use of the terms "an interaction" and " the interaction". What is the interaction? Binding? Upregulation or down regulation of one or both of the components? What is the baseline for said "interaction"? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 3 is rendered vague and indefinite by the use of the term "a said substance". Which substance is Applicant referring to? As written it is impossible to determine the metes and bounds of the claimed invention.

Claims 3, 6, 14, 15 and 17 are rendered vague and indefinite through the "administering" and "administration". It is unclear what Applicant is claiming. What is involved in said administration? How is it accomplished? What are the conditions? Is it done to a single cell or a population? As written it is impossible to determine the metes and bounds of the claimed invention.

Claim 2 is rejected as it recites improper Markush language, rendering the claim indefinite. Proper language for claim 2 would be "....selected from the from **the group consisting of** the 63 amino acid C-terminus of ICP34.5, a derivative thereof, MyD116 and GADD34."

The use of the term "homology" in claim 20 renders it vague and indefinite. It is unclear what are the parameters engendered by said term. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Claim 19 is vague and indefinite due to the use of the term "human GADD34 homologue". Is the said protein from a human or a homologue to the human GADD34 protein? As written, it is impossible to determine the metes and bounds of the claimed invention.

The use of the term "permissive" in claim 19 renders it vague and indefinite. It is unclear what the cells are permissive to. Is it HSV infection? If so section (vi) is contradictory. How can there be an HSV infection in non-permissive cells if permissiveness is defined by the ability to be infected by HSV?

Claim Rejections - 35 USC § 102

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 19 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Roizman et al. (U.S. Patent 5,834,216). Roizman et al. disclose that Herpes simplex viruses have characteristics that make them useful for the study of apoptosis. More specifically, HSV-1 encodes a gene, IPC34.5, whose function is to preclude a host response which terminates all protein synthesis subsequent to the onset of viral infection (see column 3, lines 19-28). Roizman

et al. further disclose that a stretch of 64 amino acids at the carboxyl terminus of ICP34.5 is homologous to a corresponding stretch of amino acids of the carboxyl terminus of a murine protein known as MyD116 and a Chinese hamster protein known as GADD34. Additionally, they disclose that GADD34 is structurally, closely related to MyD116, is also one of a subset of proteins induced following DNA damage or cell growth arrest (see column 3, lines 34-47). ICP34.5 has been shown to prevent the complete cessation of host cell protein synthesis replicative cycle in permissive cells infected with HSV-1. This capacity to preclude total premature shutoff of protein synthesis maps to the carboxyl terminus domain of ICP34.5 protein that is homologous to the MyD116 and GADD34 proteins (see column 3, lines 34-60) and that the carboxyl terminus of MyD116 successfully substitutes for the corresponding domain of ICP34.5. The aforementioned claims recite a "substance capable of disrupting an interaction between a ICP34.5 polypeptide or homologue thereof, or a derivative there of, and PCNA....." Since both MyD116 and GADD34 are functional and structural (with regard to the biologically-active portion carboxyl terminus) homologues of ICP34.5, they would disrupt the interaction between ICP34.5 and PCNA by competing for PCNA binding sites. In short, Roizman et al. have disclosed substances (GADD34 and MyD116) that can regulate the cell cycle of mammalian cells to prevent cell death as well as disrupt the interaction of ICP34.5 and PCNA. With regard to claims 19 and 20 which are drawn specifically to a GADD34 homologue. The GADD34 protein disclosed by Roizman et al is deemed, in absence of evidence to the contrary, to be a homologue

of the claimed GADD34 since no criteria for defining "homologues"is set forth that would preclude such a conclusion.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-13, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. (U.S. Patent 5,834,216). Roizman et al. disclose that Herpes simplex viruses have characteristics that make them useful for the study of apoptosis. More specifically, HSV-1 encodes a gene, IPC34.5, whose function is to preclude a host response which terminates all

protein synthesis subsequent to the onset of viral infection (see column 3, lines 19-28). Roizman et al. further disclose that a stretch of 64 amino acids at the carboxyl terminus of ICP34.5 is homologous to a corresponding stretch of amino acids of the carboxyl terminus of a murine protein known as MyD116 and a Chinese hamster protein known as GADD34. Additionally, they disclose that GADD34 is structurally, closely related to MyD116, is also one of a subset of proteins induced following DNA damage or cell growth arrest (see column 3, lines 34-47). ICP34.5 has been shown to prevent the complete cessation of host cell protein synthesis replicative cycle in permissive cells infected with HSV-1. This capacity to preclude total premature shutoff of protein synthesis maps to the carboxyl terminus domain of ICP34.5 protein that is homologous to the MyD116 and GADD34 proteins (see column 3, lines 34-60) and that the carboxyl terminus of MyD116 successfully substitutes for the corresponding domain of ICP34.5. Since both MyD116 and GADD34 are functional and structural (with regard to the biologically-active portion carboxyl terminus) homologues of ICP34.5, they would disrupt the interaction between ICP34.5 and PCNA by competing for PCNA binding sites. In short, Roizman et al. have disclosed substances (GADD34 and MyD116) that can regulate the cell cycle of mammalian cells to prevent cell death as well as disrupt the interaction of ICP34.5 and PCNA. Claims 7-13 are drawn to a substance capable of disrupting the interaction between ICP34.5 and PCNA affect the cell cycle of mammalian cells. Claims 19 and 20 are drawn to a homologue of GADD34 As outlined above, Roizman et al disclose that both MyD116 and

GADD34 are functional and structural homologues of ICP34.5 that can regulate the cell cycle of mammalian cells to prevent cell death as well as disrupt the interaction of ICP34.5 and PCNA.

Conclusion

No claim is allowed

Claims 1-6 and 14-18 have been found to be free of the art of record. It is suggested that claims be amended to overcome the rejections above. For example claim 1 could be amended to read as follows:

A method for identifying whether a substance inhibits the specific binding between (i) a polypeptide selected from the group consisting of herpes simplex virus (HSV) ICP34.5, the 63 amino acid C terminus of ICP34.5, MyD116, and GADD34; and (ii) proliferating cell nuclear antigen (PCNA); which comprises

(a) providing a polypeptide selected from the group consisting of herpes simplex virus (HSV) ICP34.5, the 63 amino acid C terminus of ICP34.5, MyD116, and GADD34 as a first component;

(b) providing PCNA as a second component;

(c) contacting the two components with a substance to be tested under conditions that would permit the two components to specifically bind in the absence of said substance; and

(d) determining whether said substance inhibits the specific binding between the first and second components.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Anthony Caputa, can be reached at (703)308-3995.

Robert A. Zeman

March 9, 2000

DONNA WORTMAN
PRIMARY EXAMINER